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ZIELKA, S — EXAMINER

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CATHRYN CAMPBELL
CAMPBELL AND FLORES
4370 LA JOLLA VILLAGE DRIVE
SUITE 700
SAN DIEGO CA 92122

ART UNIT	PAPER NUMBER
1804	42

1804

DATE MAILED: 04/01/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 12/2/94 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), or thirty (30) days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 3,4,8,9,11,12,16-18,21-29 are pending in the application.
   Of the above, claims 3,4,8,9,11,12,16-18 are withdrawn from consideration.
2. ☒ Claims 1,2,5-7,10,13-15,19,20 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 21-29 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

This application should be reviewed for errors.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, 5-7, 10, 13-15, 19, 20 and 26 have been cancelled; claims 3, 4, 8, 9, 11, 12 and 16-18 have been withdrawn from consideration as being directed to a non-elected invention.

Newly submitted claims 30-34 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: newly added claims 31-34 now claim subject matter not originally examined. The newly added claims now differentiate between TGF-beta "activity" and the induction of ECM in response to TGF-beta induction. The election of treatment using antibodies is carried over from the parent application; applicants elected the body treatment using antibodies in the response to the restriction requirement of paper 11, mailed 7/03/91. Claim 31 is not directed to a method of treating a pathology and therefore constitutes a new invention. A search of the claimed subject matter, inhibition of autocrine expression, does not over lap with a search of therapy claims and therefore constitutes divergent subject matter necessitating a separate search.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 31-34 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 21-25, 27-29 and 30 are active and examined in this Office Action.

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on October 7, 1996, has been entered.

The declaration of Drs. Border and Ruoslahti is acknowledged, has been considered and is addressed, below.

The provisional rejection of claims 21-25 and 27-30 under the judicially created doctrine of obviousness type double patenting as being unpatentable over the claims of copending application serial no. 07/803,285 is maintained. Applicants have held this issue in abeyance.

The provisional rejection of claims 21-25 and 27-30 under the judicially created doctrine of obviousness type double patenting as being unpatentable over the claims of copending application serial no. 07/467,888 is maintained. Applicants have held this issue in abeyance.

The rejection of claims 21-25 and 27-30 under 35 U.S.C. 112, first paragraph and second paragraphs, is maintained. Applicants are reminded that the antibodies as the agent was elected in the response to the restriction requirement and the claims should be so limited. Claims 21 and 27 are not so limited. The word "agent" reads on a soluble receptor, for example, and therefore the word "agent" remains vague and unclear. The specification has literal support for only an anti-TGF-beta antibody, a PDGF and an RGD-containing peptide. While the claims are to be interpreted in light of the specification, they are not so limited and the word "agent" further reads on any general protein synthesis inhibitor.

Applicants have argued on pages 11-15 that the Office is challenging the operability or utility of the methods of the invention as useful and efficacious treatments. However, contrary to such arguments, the rejection is not a 101 utility rejection but one of enablement. The specification fails to enable one of skill to practice the invention as claimed using other agents and arguments pertaining a utility rejection will not be addressed. Applicant's arguments from pages 11-15 pertaining to the PDGF and RGD containing peptide will also not be addressed as that subject matter was removed from consideration as being drawn to a non-elected invention. The specification must describe and enable the invention as claimed; hypothetical agents which may act in a similar manner to the anti-TGF-beta antibody are not described or enabled in the specification.

Applicants have argued at pages 16-20 that the claims need not be limited to decorin or byglycan and that the claims as now amended read on a method of treating a pathology or a condition characterized by the TGF-beta induced production of an ECM component in a tissue. However, the claims claim an ECM component and since a component is claimed, the component must be limited to decorin or biglycan. Applicant's arguments are not commensurate with the scope of the claim. Applicants may wish to claim only "ECM".

Applicants have argued at pages 20-29 that the claims are enabled for treatment of cirrhosis and ARD. However, the specification fails to working examples or other evidence that cirrhosis or ARD is solely the result of increased TGF-beta expression; the fact remains that both pathologies may be caused by non-TGF-beta related events. Establishment of a nexus between the results obtained in the specification and the claimed embodiments is necessary to overcome the rejection. Contrary to applicant's arguments, the phraseology "treating a pathology or a

condition" inherently implies some relevant biological effect and therefore the disclosure must enable a "treatment regimen" or "evidence of effects of treatment". The examiner suggests language such as "a method of decreasing the accumulation of ECM"....to remove the treatment/cure considerations.

Applicant's arguments regarding the effective treatment versus method to claim to cure a disease or treat all phases of a progressive chronic disease are not persuasive. The phraseology "a method of treating a pathology or a condition" requires enablement at any stage and the specification is not enabling for treatment of progressive diseases not characterized at all stages by TGF-beta expression. The claims can be rewritten to overcome the rejection but the rejection stands on the claims as written.

Applicant's arguments drawn to the use of the peptides will not be addressed as those arguments are directed to non-elected subject matter.

Applicant's arguments concerning manipulating the specific effect of TGF-beta and that this has utility in controlling or the undesirable accumulation of ECM are persuasive but the arguments are not commensurate with the scope of the claims.

Regarding the rejection under 35 U.S.C. 112, second paragraph, concerning the word "agent", the rejection is maintained for reasons set forth above. Applicants are reminded that although claims are to be interpreted in light of the specification, the claims are not so limited. The word "agent" remains vague and unclear.

The rejection of claim 27 under 35 U.S.C. 102(b) as being anticipated by Flanders is withdrawn in view of the amendments to the claims.

The rejection of claims 21, 24 and 27-30 under 35 U.S.C. 103 as being unpatentable over Connor is maintained. Regarding the declaration, the declaration is insufficient to overcome the

rejection since the declaration shows the generation of antibodies to TGF-beta and the inhibition of TGF-beta in cell culture. The rejection over Connor addresses the in vivo treatment therapy and the declaration is not commensurate with the scope of the claims.

The rejection of claims 22, 23, 25 under 35 U.S.C. 103 as being unpatentable over Connor as applied to claims 21 and 24 above and further in view of McKay is maintained.Regarding the declaration, the declaration is insufficient to overcome the rejection since the declaration shows the generation of antibodies to TGF-beta and the inhibition of TGF-beta in cell culture. The rejection over Connor addresses the in vivo treatment therapy and the declaration is not commensurate with the scope of the claims.

The rejection of claims 29 and 30 under 35 U.S.C. 103 as being unpatentable over Flanders as applied to claim 27 above and further in view of Bassols is withdrawn in view of the withdrawal of the rejection of claim 27, above.

The following new grounds of rejection are necessitated by applicant's amendments to the claims.

Claims 21-25 and 27-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Regarding claim 21, the claim has been amended to now claim "A TGF-beta" as opposed to formerly "TGF-beta". The specification is not enabling for differentiation between TGF B1, B2 or B3 and the use of antibodies or agents directed specifically and solely thereto. The inclusion of the new claim language constitutes the addition of new matter and Applicants have not specifically pointed out

support for these amendments to the claims. Further regarding claim 21, the addition of the claim language "binding of the agent" now directly reads on a soluble receptor for which the specification is not enabling. The specification further fails to distinguish between a "condition" and a "pathology" and the specification fails to provide guidance to one of skill to determine when the expression of TGF-beta results in a condition versus a pathology.

Regarding claim 27, the claim has now been amended to claim "activity", "A TGF-beta" as opposed to formerly "TGF-beta" and now distinguishes between TGF-beta activity per se and the ECM inducing activity of TGF-beta in view of the use of "or". The specification is not enabling for differentiation between TGF B1, B2 or B3 and the use of antibodies or agents directed specifically and solely thereto. The inclusion of the new claim language constitutes the addition of new matter and Applicants have not specifically pointed out support for these amendments to the claims. The "activity" phraseology is undefined by the specification and is only related to the presence/absence or ECM production. The specification fails to provide enablement for determination of "activity" per se; TGF-beta expression is related to ECM expression and the specification fails to provide enablement for separating the two phenomena.

Limitation of the claims to mesangial cells, kidney tissue, ECM, use of antibodies as the agent and amendments to the claims in view of the rejections above would overcome the rejections.

No claim is allowed.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO FAX center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (30 November 15, 1989). The CM1 Fax Center number is (703) 305-3014 or (703) 308-0294.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Suzanne Ziska, Ph.D., whose telephone number is (703)308-1217. In the event the examiner is not available, the examiner's supervisor, Ms. Jacqueline Stone, may be contacted at phone number (703) 308-3153.

SUZANNE E. ZISKA
PRIMARY EXAMINER
GROUP 1800